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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,542	03/02/2007	David Wallach	WALLACH34	3237

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EXAMINER	
STOICA, ELLY GERALD	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
11/08/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,542	WALLACH ET AL.	
	Examiner	Art Unit	
	ELLY-GERALD STOICA	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-58 and 60* is/are pending in the application.

4a) Of the above claim(s) *26-58 and 60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of the specie antibody capable of binding to the amino acid sequence at amino acid coordinates 123-175 of SEQ ID NO: 3 (SIVA1), in the reply filed on 10/29/2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 21-58 and 60 are pending; claims 26-58 and 60 are withdrawn in view of the previous restriction requirement and the species election. Claims 21-25 are currently examined.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 21-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of an immune disorder by administering an antibody that binds the region comprised by the amino acid residues 123-175 of SEQ ID NO: 3, does not reasonably provide enablement for treatment in the case of expressing the treating agent within the cells of said individual. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are drawn to a method of treating an immune disorder comprising administering to an individual having the immune disorder a therapeutically effective amount of an agent capable of increasing or decreasing NF-KB inducing kinase (NIK)-SIVA complex formation, thereby treating the immune disorder in the individual, wherein said agent is an antibody capable of binding to the amino acid sequence at amino acid coordinates 123-175 of SEQ ID NO: 3 (SIVI). The disorder is characterized by an abnormal function or level of Blys, CD27, SIVA or NIK. Further limitation address the possibility of treatment in the case of expressing the treating agent within the cells of said individual (Lymphocyte cells).

While the art recognizes the possibility of delivering antibodies against intracellular proteins into the cell, expressing the intrabody into the cell raises a series of challenges. A major challenge for the successful application of intrabodies for therapy is achieving sufficient expression inside target cells. Different approaches are applicable to cells *in vitro* compared with delivery of intrabodies to cells *in vivo* for the treatment of

disease. Virally mediated gene transfer for intracellular intrabody synthesis (Fig 4c) might be an option, because this method can yield a continuous supply of antibody. An alternative approach would be to use immuno liposomes lipid bilayer formulations that can encompass nucleic acids and could carry an intrabody expression vector to the desired site of action. The specificity of delivery relies on antibody fragments, such as scFv, on the surface of the immunoliposomes that are specific for a surface antigen on the target cell (Fig 4d).This approach could target an intrabody to tumor cells, or to other disease-associated targets, expressing known markers thereby promoting internalization of an intrabody vector. These methods are promising, but there are major problems to be overcome (Lobato et al., Intracellular antibodies and challenges facing their use as therapeutic agents. Trends Mol. Med. 9, 390-396, 2003).

The specification does not provide any guidance with regard to the possibility of expressing the antibody in the cells of the subject to be treated and no working examples are described. Thus in order to achieve this particular type of treatment a vast amount of experimentation in an unpredictable territory of therapeutics would be necessary.

Due to the large quantity of experimentation necessary to test the possibility of using intrabody expression in an *in vivo* setting; the lack of direction/guidance presented in the specification regarding this particular method of treatment; the absence of working examples directed to same; the state of the prior art which establishes the unpredictability of the in vivo treatment by expressing intrabodies in patient's own cells;

undue experimentation would be required of the skilled artisan to use the claimed invention in its full scope.

Claim Rejections - 35 USC § 102/103

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 21-23 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kanteti et al. (WO/1998/543323- cited by Applicant).

Kanteti et al. teach SIVA protein can or portions or fragments thereof, can be used to prepare anti-Siva antibodies. The fragment may be as short as 8 amino acids and preferably at least 30 amino acids in length and encompasses an epitope of Siva such that an antibody raised against the peptide forms a specific immune complex with Siva; the antibody is incorporated into a pharmaceutical composition comprising the antibody and a pharmaceutically acceptable carrier (p. 6, lines 24-35). Also taught are

methods of treating methods for treating subjects having various disorders characterized by aberrant Siva protein activity such as a proliferative disorder of an immune cell, or an autoimmune disease , Non-Hodgkin's lymphomas, Hodgkin's disease, leukemias such as acute and chronic leukemias and other immune cells disorders, multiple sclerosis, myasthenia gravis, systemic lupus erythematosis, Sjogren's Syndrome, administering to the subject a Siva antibody such that treatment of the subject occurs (p.50, line 21to p. 51 line 9)

The examiner is unable to determine whether the prior art disclosures actually possesses the characteristics of the antibodies of the instant Application. Under such circumstances, where the product seems to be identical, then the burden shifts to applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. Note the case law of In re Best 195 USPQ 430, 433 (CCPA 1977).

Conclusion

7. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ELLY-GERALD STOICA whose telephone number is (571)272-9941. The examiner can normally be reached on 9:00-18:30 M-Th and 9:00-18:30 alternate F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Elly-Gerald Stoica/
Examiner, Art Unit 1647